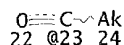


Attempt to cover claim 1 | packet #1

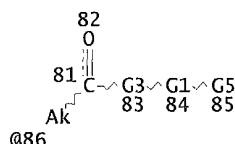
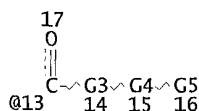
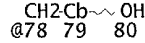
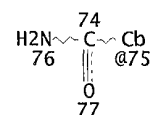
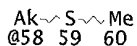
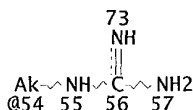
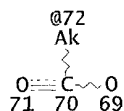
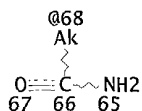
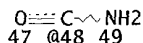
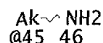
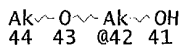
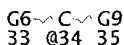
KAM 09/926,391

=> d que 191
L18

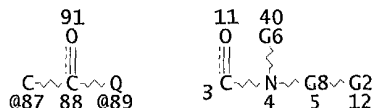
STR



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Page 1-A



Page 2-A

REP G1=(0-1) 87-83 89-85

VAR G2=86/13

VAR G3=N/O

REP G4=(0-1) 87-14 89-16

VAR G5=H/23/25/26/42

VAR G6=H/25

VAR G8=CH2/34

VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 24

CONNECT IS E1 RC AT 25

CONNECT IS E2 RC AT 26

CONNECT IS E2 RC AT 42

CONNECT IS E1 RC AT 44

CONNECT IS E2 RC AT 54

CONNECT IS E2 RC AT 58

CONNECT IS E1 RC AT 62

CONNECT IS E1 RC AT 64

CONNECT IS E2 RC AT 68

CONNECT IS E1 RC AT 69

CONNECT IS E2 RC AT 72

CONNECT IS E2 RC AT 75

CONNECT IS E2 RC AT 79

CONNECT IS E2 RC AT 86

DEFAULT MLEVEL IS ATOM

GGCAT IS UNS AT 62

GGCAT IS MCY UNS AT 64

GGCAT IS MCY UNS AT 75

GGCAT IS MCY UNS AT 79

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS X3 C AT 42

ECOUNT IS X2 C AT 52

ECOUNT IS E2 C AT 58

claim 1 is really
broad. I did a
number of iterations
but there are still
a lot of cpds.

I limited by
crossing w/ melanin
& di- or tripeptide
& date. see p 7

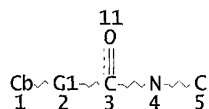
the cpds in the
cites aren't great.
I labeled the cpds
as good or bad.

I decided to search
claim 2. see packet
#2

ECOUNT IS M3-X8 C X2 N AT 62
 ECOUNT IS E6 C AT 64
 ECOUNT IS X2 C AT 68
 ECOUNT IS X2 C AT 72
 ECOUNT IS E6 C AT 75
 ECOUNT IS E6 C AT 79

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 70

STEREO ATTRIBUTES: NONE
 L40 STR

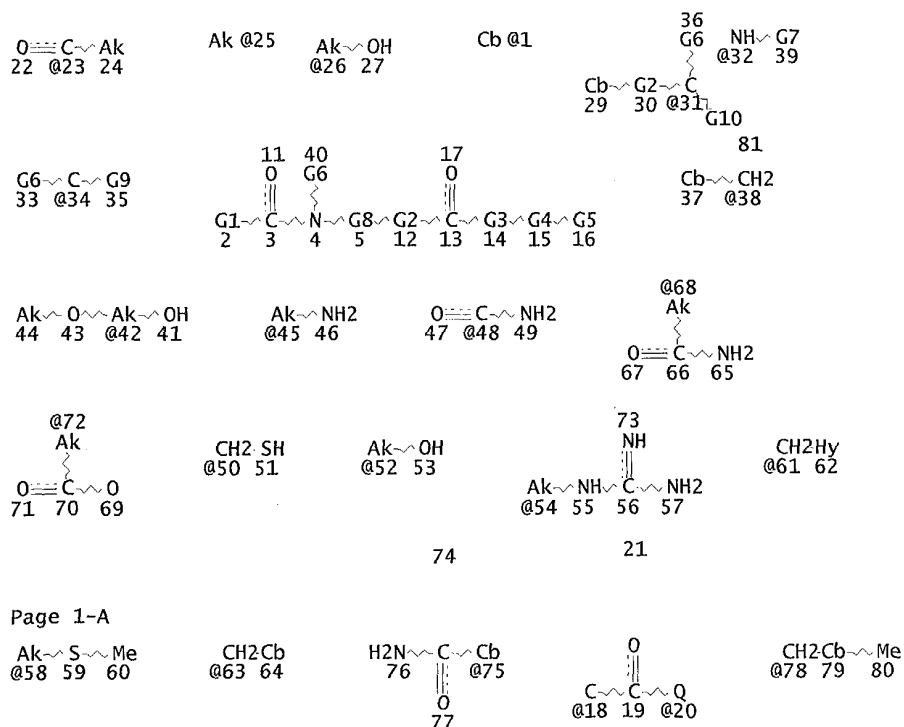


REP G1=(0-7) C
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 GG CAT IS PCY UNS AT 1
 DEFAULT ECLEVEL IS LIMITED
 ECOUNT IS E10 C AT 1

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 6

STEREO ATTRIBUTES: NONE

L41 (513628)SEA FILE=REGISTRY ABB=ON PLU=ON 591.49.57/RID
 L42 (32652)SEA FILE=REGISTRY SUB=L41 SSS FUL L40
 L43 STR



Page 1-A

Page 2-A

VAR G1=1/31/38

REP G2=(0-6) C

VAR G3=N/O

REP G4=(0-1) 18-14 20-16

VAR G5=H/23/25/26/42

VAR G6=H/25

VAR G7=23/25/26/42

VAR G8=CH2/34

VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78

VAR G10=NH2/32

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 24

CONNECT IS E1 RC AT 25

CONNECT IS E2 RC AT 26

CONNECT IS E2 RC AT 42

CONNECT IS E1 RC AT 44

CONNECT IS E2 RC AT 54

CONNECT IS E2 RC AT 58

CONNECT IS E1 RC AT 62

CONNECT IS E1 RC AT 64

CONNECT IS E2 RC AT 68

CONNECT IS E1 RC AT 69

CONNECT IS E2 RC AT 72

CONNECT IS E2 RC AT 75

CONNECT IS E2 RC AT 79

DEFAULT MLEVEL IS ATOM

GGCAT IS PCY UNS AT 1

GGCAT IS PCY UNS AT 29

GGCAT IS PCY UNS AT 37

GGCAT IS UNS AT 62

GGCAT IS MCY UNS AT 64

GGCAT IS MCY UNS AT 75

GGCAT IS MCY UNS AT 79

DEFAULT ELEVEL IS LIMITED

ECOUNT IS E10 C AT 1

ECOUNT IS E10 C AT 29

ECOUNT IS E10 C AT 37

ECOUNT IS X3 C AT 42

ECOUNT IS X2 C AT 52

ECOUNT IS E2 C AT 58

ECOUNT IS M3-X8 C X2 N AT 62

ECOUNT IS E6 C AT 64

ECOUNT IS X2 C AT 68

ECOUNT IS X2 C AT 72

ECOUNT IS E6 C AT 75

ECOUNT IS E6 C AT 79

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 75

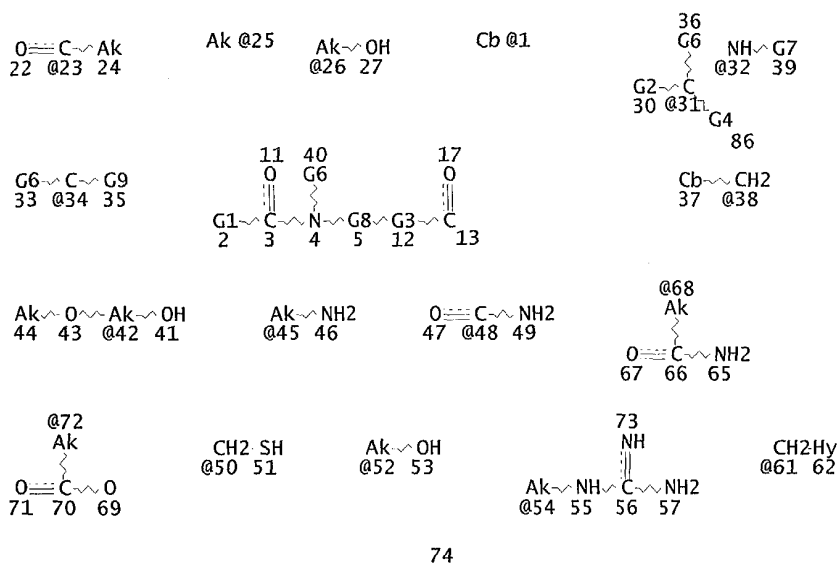
STEREO ATTRIBUTES: NONE

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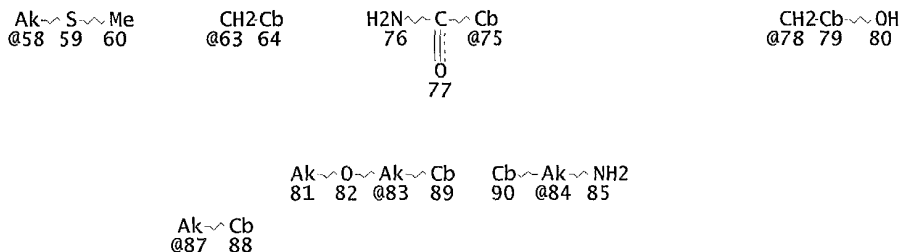
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L46 2701 SEA FILE=REGISTRY SUB=L45 SSS FUL L18

L53 STR



Page 1-A



Page 2-A

VAR G1=1/31/38
 VAR G2=1/87/83/84
 REP G3=(0-6) C
 VAR G4=NH2/32
 VAR G6=H/25
 VAR G7=23/25/26/42
 VAR G8=CH2/34
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NODE ATTRIBUTES:

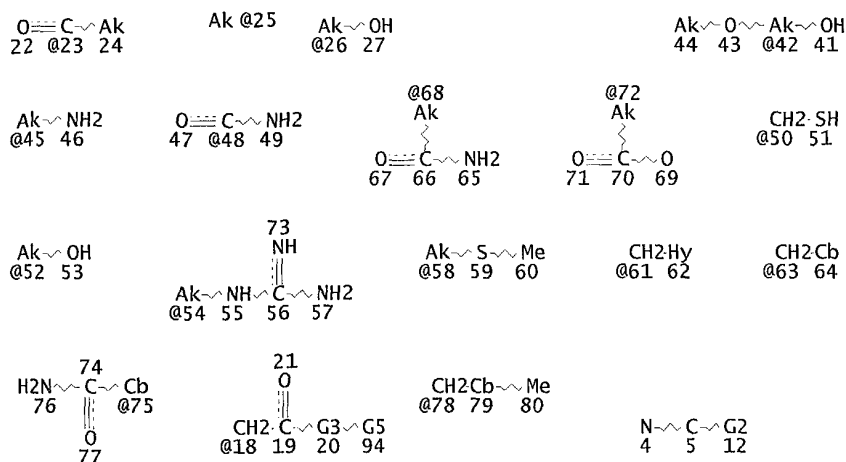
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 CONNECT IS E1 RC AT 24
 CONNECT IS E1 RC AT 25
 CONNECT IS E2 RC AT 26
 CONNECT IS E1 RC AT 37
 CONNECT IS E3 RC AT 42
 CONNECT IS E1 RC AT 44
 CONNECT IS E2 RC AT 45
 CONNECT IS E2 RC AT 54
 CONNECT IS E2 RC AT 58
 CONNECT IS E1 RC AT 62
 CONNECT IS E1 RC AT 64
 CONNECT IS E2 RC AT 68
 CONNECT IS E1 RC AT 69
 CONNECT IS E2 RC AT 72
 CONNECT IS E2 RC AT 75

CONNECT IS E2 RC AT 79
 CONNECT IS E1 RC AT 81
 CONNECT IS E2 RC AT 87
 DEFAULT MLEVEL IS ATOM
 GGCAT IS PCY UNS AT 1
 GGCAT IS PCY UNS AT 37
 GGCAT IS UNS AT 62
 GGCAT IS MCY UNS AT 64
 GGCAT IS MCY UNS AT 75
 GGCAT IS MCY UNS AT 79
 GGCAT IS PCY UNS AT 88
 GGCAT IS PCY UNS AT 89
 GGCAT IS PCY UNS AT 90
 DEFAULT ELEVEL IS LIMITED
 ECOUNT IS E10 C AT 1
 ECOUNT IS E10 C AT 37
 ECOUNT IS X3 C AT 42
 ECOUNT IS X2 C AT 52
 ECOUNT IS E2 C AT 58
 ECOUNT IS M3-X8 C X2 N AT 62
 ECOUNT IS E6 C AT 64
 ECOUNT IS X2 C AT 68
 ECOUNT IS X2 C AT 72
 ECOUNT IS E6 C AT 75
 ECOUNT IS E6 C AT 79
 ECOUNT IS E10 C AT 88
 ECOUNT IS E10 C AT 89
 ECOUNT IS E10 C AT 90

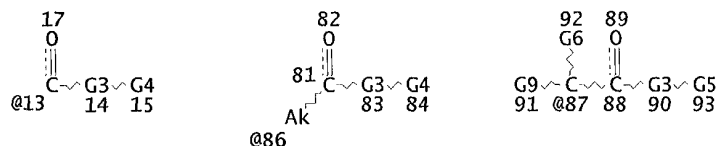
GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 76

STEREO ATTRIBUTES: NONE

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 N O OR C S)/RELF
 L59 1551 SEA FILE=REGISTRY ABB=ON PLU=ON L58 NOT (M/ELS OR B/ELS OR
 SI/ELS OR NC5/ESS OR N2C3/ES OR "NITRO" OR "HYDROXYAMINO")
 L61 1405 SEA FILE=REGISTRY ABB=ON PLU=ON L59 AND 1 591.49.57/RID
 L62 1383 SEA FILE=REGISTRY ABB=ON PLU=ON L61 NOT ("FLUOREN" OR
 "TRICYCLO")
 L63 1259 SEA FILE=REGISTRY ABB=ON PLU=ON L62 NOT X/ELS
 L64 1234 SEA FILE=REGISTRY ABB=ON PLU=ON L63 AND NC=1 NOT NC6/ESS
 L68 1202 SEA FILE=REGISTRY ABB=ON PLU=ON L64 NOT (P/ELS OR OC5/ES)
 L76 STR



Page 1-A



Page 2-A

VAR G2=13/86

VAR G3=NH/O

VAR G4=H/23/25/26/42/87/18

VAR G5=H/23/25/26/42

VAR G6=H/25

VAR G9=25/NH2/45/68/72/48/75/63/58/50/52/54/61/78

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 24

CONNECT IS E1 RC AT 25

CONNECT IS E2 RC AT 26

CONNECT IS E3 RC AT 42

CONNECT IS E1 RC AT 44

CONNECT IS E2 RC AT 54

CONNECT IS E2 RC AT 58

CONNECT IS E1 RC AT 62

CONNECT IS E1 RC AT 64

CONNECT IS E2 RC AT 68

CONNECT IS E1 RC AT 69

CONNECT IS E2 RC AT 72

CONNECT IS E2 RC AT 75

CONNECT IS E2 RC AT 79

CONNECT IS E2 RC AT 86

DEFAULT MLEVEL IS ATOM

GGCAT IS UNS AT 62

GGCAT IS MCY UNS AT 64

GGCAT IS MCY UNS AT 75

GGCAT IS MCY UNS AT 79

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS X3 C AT 42

ECOUNT IS X2 C AT 52

ECOUNT IS E2 C AT 58

ECOUNT IS M3-X8 C X2 N AT 62

ECOUNT IS E6 C AT 64

ECOUNT IS X2 C AT 68

KAM 09/926,391

ECOUNT IS X2 C AT 72
ECOUNT IS E6 C AT 75
ECOUNT IS E6 C AT 79

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 70

STEREO ATTRIBUTES: NONE

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INYL" OR C O/RELF)
L86 1037 SEA FILE=REGISTRY ABB=ON PLU=ON L85 NOT ("BENZODIAZEPIN" OR
"NITRILE" OR "CYANO" OR "FORMYL")
L87 425 SEA FILE=CAPLUS ABB=ON PLU=ON L86
L88 9 SEA FILE=CAPLUS ABB=ON PLU=ON L87 AND ?MELAN? *use*
L89 28 SEA FILE=CAPLUS ABB=ON PLU=ON L87 AND (DIPEPTIDE OR TRIPEPTID
E)/OBI
L90 35 SEA FILE=CAPLUS ABB=ON PLU=ON (L88 OR L89)
L91 25 SEA FILE=CAPLUS ABB=ON PLU=ON L90 AND PY<2001 *← limited by data*

=> d ibib abs hitstr 1-10

L91 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:312019 CAPLUS

DOCUMENT NUMBER: 136:325828

TITLE: Preparation of dipeptide derivatives as cell adhesion inhibitors

INVENTOR(S): Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng; Castro, Alfredo C.; Zimmerman, Craig N.; Hammond, Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan; Singh, Juswinder

PATENT ASSIGNEE(S): Biogen, Inc., USA

SOURCE: U.S., 50 pp., Cont.-in-part of U.S. 6,306,840.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

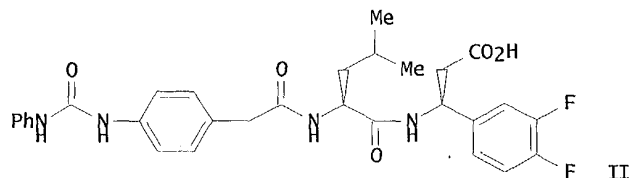
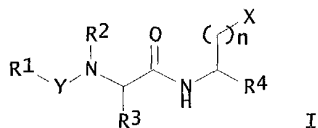
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376538	B1	20020423	US 1997-875321	19970919
US 6306840	B1	20011023	US 1995-376372	19950123
WO 9622966	A1	19960801	WO 1996-US1349	19960118 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
EP 1142867	A2	20011010	EP 2001-107877	19960118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
US 2003018016	A1	20030123	US 2001-2341	20011023
PRIORITY APPLN. INFO.:			US 1995-376372	A2 19950123
			WO 1996-US1349	W 19960118
			EP 1996-905316	A3 19960118
			US 1997-875321	A3 19970919

OTHER SOURCE(S): MARPAT 136:325828

GI



AB Novel dipeptide analogs I [X = CO₂H, PO₃H⁻, SO₂R₅, SO₃H, OPO₃H⁻, CO₂R₄; Y = CO, SO₂, PO₂; n = 0-2; R₁ = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl, alkoxy, alkenyloxy, aralkoxy, alkylamino, alkenylamino,

alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, heterocyclyl; R2 = H, aryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aralkyl; R2NCR3 = heterocyclic ring; R3 = natural, unnatural, modified, or substituted amino acid side chain; R4 = optionally substituted aryl, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aralkyl, H, heterocyclyl, heterocyclylcarbonyl, aminocarbonyl, amido, alkylaminocarbonyl, arylaminocarbonyl, acylaminocarbonyl, acyl; R5 = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl] are prepd. as compds. useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical compds. of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, .beta.-amino acid-contg. dipeptide II, prepd. by std. methods, displayed an IC50 of <50 nM in a cell adhesion inhibition assay.

IT 181520-01-4P 181520-03-6P 181520-87-6P

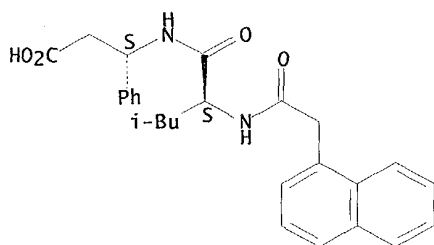
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of .beta.-amino acid dipeptide derivs. as cell adhesion inhibitors)

RN 181520-01-4 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(1-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

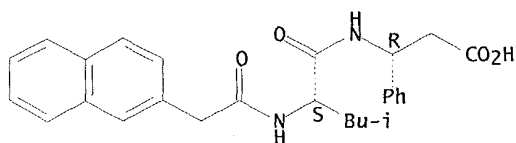
Absolute stereochemistry.



RN 181520-03-6 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

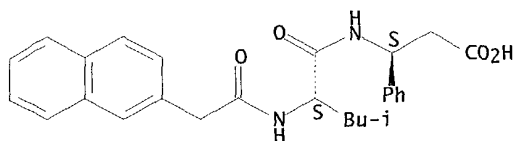
Absolute stereochemistry.



RN 181520-87-6 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 181518-17-2P 181518-19-4P

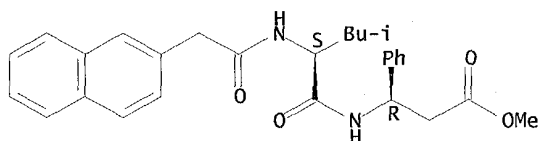
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of .beta.-amino acid dipeptide derivs. as cell adhesion inhibitors)

RN 181518-17-2 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.R)-(9CI) (CA INDEX NAME)

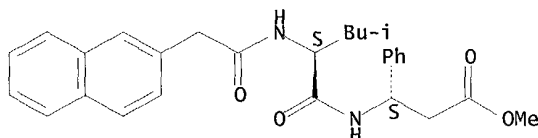
Absolute stereochemistry.



RN 181518-19-4 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:366736 CAPLUS

DOCUMENT NUMBER: 134:340711

TITLE: Preparation of tripeptide .alpha.-ketoamides as serine and cysteine protease inhibitors

INVENTOR(S): Powers, James C.

PATENT ASSIGNEE(S): Georgia Tech Research Corp., USA

SOURCE: U.S., 24 pp., Cont.-in-part of U.S. 5,650,508.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

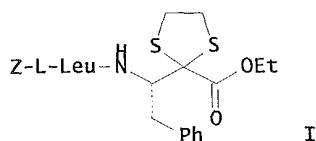
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235929	B1	20010522	US 1996-777354	19961227
US 5650508	A	19970722	US 1995-539944	19951006 <--
PRIORITY APPLN. INFO.:			US 1991-815073	B1 19911227
			US 1993-118997	B1 19930909

KAM 09/926,391

US 1994-246511 B1 19940520
US 1995-539944 A2 19951006

OTHER SOURCE(S): MARPAT 134:340711
GI



AB Tripeptide .alpha.-ketoamides M1-AA1-AA2-AA3-CONR3R4 [M1 = H, NH2CO, NH2CS, NH2SO2, XNHCO, X2NCO, XNHCS, X2NCS, XNHSO2, X2NSO2, XCO, XCS, XSO2, XO2C, XOCS; X = (un)substituted C1-10 alkyl or fluoroalkyl, 1-adamantyl, 9-fluorenyl, (un)substituted Ph or naphthyl; AA1 and AA2 = independently side-chain (un)blocked amino acid selected from alanine, valine, leucine, isoleucine, glycine, serine, aspartic acid, and glutamic acid; AA3 = aspartic or glutamic acid; R3 = alkyl or cycloalkyl substituted by Ph and optionally other substituents; R4 = H, alkyl or cycloalkyl which may have a Ph group and other substituents] were prepd. as serine and cysteine protease inhibitors. Thus, condensation of protected peptidyl ketoester I (Z = PhCH2O2C) (prepd. in 3 steps from Z-Leu-Phe-OH, Et oxalyl chloride, and 1,2-ethanedithiol) with alkylamines RNH2 (R = Et, Pr, Bu, Bu-i, CH2Ph, CH2CH2Ph) gave peptidyl ketoamides Z-Leu-Phe-CONHR (II). Peptidyl ketoamides II inhibited chymotrypsin with Ki = 8-73 .mu.M and had half-lives in liver and plasma of >60.

IT 170902-24-6

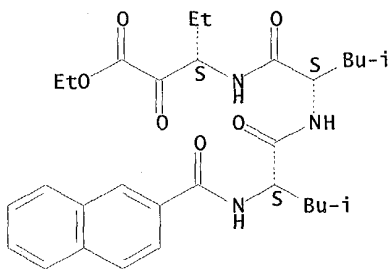
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of peptide ketoamides as serine and cysteine protease inhibitors)

RN 170902-24-6 CAPLUS

CN L-Leucinamide, N-(2-naphthalenylcarbonyl)-L-leucyl-N-[(1S)-3-ethoxy-1-ethyl-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:772657 CAPLUS

DOCUMENT NUMBER: 133:329599

TITLE:

INVENTOR(S): Melanocyte-stimulating hormone inhibitors
Shiojiri, Eiji; Takino, Yoshinobu; Chujou, Hiromi;
Sakamoto, Kazutami; Ijichi, Chiori; Eto, Yuzuru;
Iwasaki, Keiji

PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan

SOURCE: PCT Int. Appl., 37 pp.

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064926	A1	20001102	WO 2000-JP2687	20000425 <--
W: CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1174437	A1	20020123	EP 2000-917447	20000425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

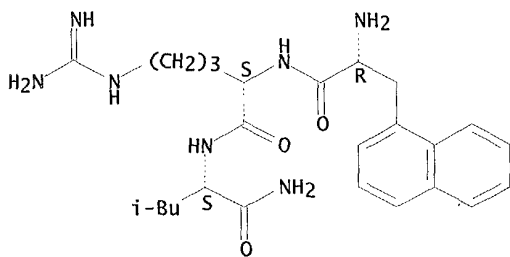
PRIORITY APPLN. INFO.: JP 1999-118633 A 19990426
 WO 2000-JP2687 W 20000425

AB MSH inhibitors characterized by contg., as the active ingredient, di- or tripeptide derivs. having a specific naphthyl group or salts thereof, or a MSH inhibiting compd. showing a 50% inhibitory concn. (IC50) on cAMP prodn. of 100 nm or less. These inhibitors can inhibit pigmentation, prevent, ameliorate or treat immunopathy or immunodeficiency, or regulate body wt. by controlling appetite. These inhibitors are usable in cosmetics and skin preps. for external use. Moreover, they can be easily produced and have a high storage stability.

IT 303728-46-3P 303728-47-4P 303728-48-5P 303728-49-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (di- and tripeptide derivs. as MSH inhibitors)

RN 303728-46-3 CAPLUS
 CN L-Leucinamide, 3-(1-naphthalenyl)-D-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

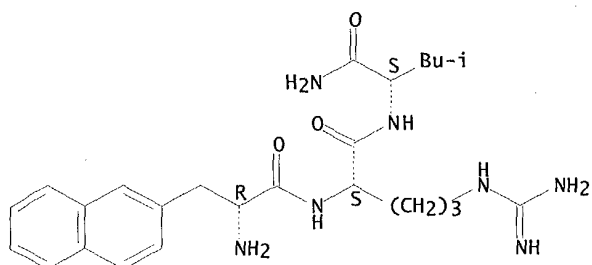
Absolute stereochemistry.



*cpds shown in
 appl. work are novel*

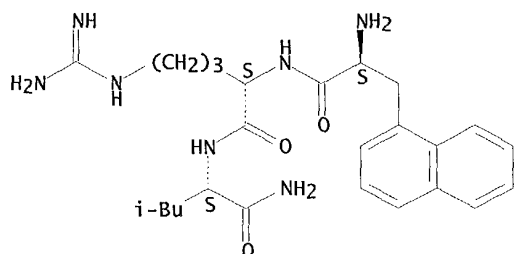
RN 303728-47-4 CAPLUS
 CN L-Leucinamide, 3-(2-naphthalenyl)-D-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



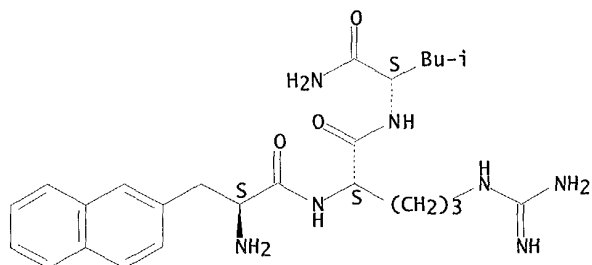
RN 303728-48-5 CAPLUS
 CN L-Leucinamide, 3-(1-naphthalenyl)-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 303728-49-6 CAPLUS
 CN L-Leucinamide, 3-(2-naphthalenyl)-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2000:439425 CAPLUS
 DOCUMENT NUMBER: 133:204542
 TITLE: **Dipeptide** formation on engineered hybrid peptide synthetases
 AUTHOR(S): Doekel, Sascha; Marahiel, Mohamed A.
 CORPORATE SOURCE: Philipps-Universität, Fachbereich Chemie/Biochemie, Marburg, 35032, Germany
 SOURCE: Chemistry & Biology (2000), 7(6), 373-384
 CODEN: CBOLE2; ISSN: 1074-5521
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: Nonribosomal peptide synthetases (NRPSs) are modular megaenzymes that catalyze the assembly of a large no. of bioactive peptides using the multiple carrier thiotemplate mechanism. The modules comprise specific domains that act as distinct units to catalyze specific reactions assocd. with substrate activation, modification and condensation. Such an arrangement of biosynthetic templates has evoked interest in engineering novel NRPSs. Results: We describe the design and construction of a set of dimodular hybrid NRPSs. By introducing domain fusions between adenylation and thiolation (PCP) domains we designed synthetic templates for dipeptide formation. The predicted dipeptides, as defined by the specificity and arrangement of the adenylation domains of the constructed templates, were synthesized *in vitro*. The effect of the intramol. fusion was investigated by detg. kinetic parameters for substrate adenylation and thiolation. The rate of dipeptide formation on the artificial NRPSs is similar to that of natural templates. Conclusions: Several new aspects concerning the tolerance of NRPSs to domain swaps can be deduced. By choosing the fusion site in the border region of adenylation and PCP domains we showed that the PCP domain exhibits no general substrate selectivity. There was no suggestion that selectivity of the condensation reaction was biased toward the donor amino acid, whereas at the acceptor position there was a size-detd. selection. In addn., we demonstrated that a native elongation module can be converted to an initiation module for peptide-bond formation. These results represent the first example of rational *de novo* synthesis of small peptides on engineered NRPSs.

IT 290298-01-0P

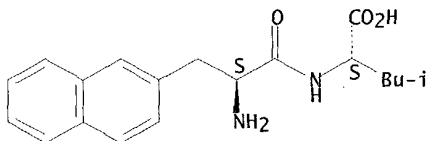
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(dipeptide formation on engineered hybrid nonribosomal peptide synthetases)

RN 290298-01-0 CAPLUS

CN L-Leucine, 3-(2-naphthalenyl)-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2000:84636 CAPLUS
 DOCUMENT NUMBER: 132:141955
 TITLE: Encapsulation of water soluble peptides
 INVENTOR(S): Ignatious, Francis X.
 PATENT ASSIGNEE(S): Biomeasure Incorporated, USA
 SOURCE: PCT Int. Appl., 33 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004916	A1	20000203	WO 1999-US14869	19990709 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,				

TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2338345	AA	20000203	CA 1999-2338345	19990709	<--
AU 9949646	A1	20000214	AU 1999-49646	19990709	<--
EP 1098660	A1	20010516	EP 1999-933630	19990709	
EP 1098660	B1	20021016			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002521343	T2	20020716	JP 2000-560909	19990709	
EP 1240896	A2	20020918	EP 2002-76666	19990709	
EP 1240896	A3	20030326			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
AT 226083	E	20021115	AT 1999-933630	19990709	
ES 2185373	T3	20030416	ES 1999-933630	19990709	
US 6270700	B1	20010807	US 1999-357453	19990720	
NO 2001000358	A	20010322	NO 2001-358	20010122	
PRIORITY APPLN. INFO.:			US 1998-121653	A1	19980723
			US 1998-93914P	P	19980723
			EP 1999-933630	A3	19990709
			WO 1999-US14869	W	19990709

AB This invention relates to a process for prepg. biodegradable microspheres and/or nanospheres using an oil-in-water process for the controlled release of bioactive peptides. Thus, of poly(dl-lactide-co-glycolide) (70:30) was mixed with 2% malic acid. NaHCO₃ (1N) was added to the polymer and mixed with an aq. soln. of the acetate salt of pyroGlu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH₂. Soln. The soln. was stirred for about 2 h and pptd. in 400 mL cold water kept at about 4-6.degree.. The above vacuum dried complex was dissolved in CH₂Cl₂ (DCM) and the soln. was mixed with 1% PVA soln. The DCM was evapd. off, and the microspheres were collected by centrifugation, suspended in water and lyophilized.

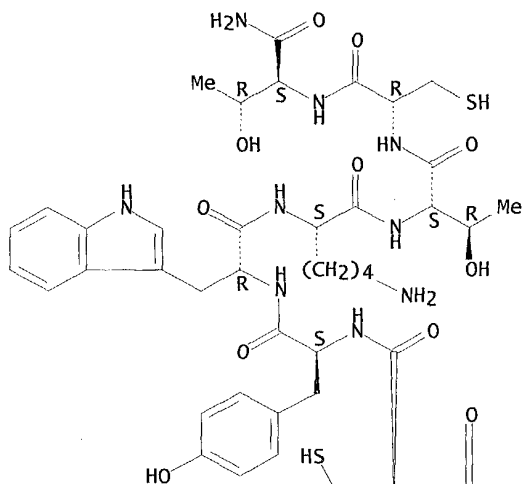
IT 150996-95-5
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (encapsulation of water sol. peptides)

RN 150996-95-5 CAPLUS

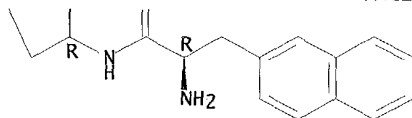
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



too long

L91 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:325961 CAPLUS

DOCUMENT NUMBER: 130:352553

TITLE: Synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins

INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry

PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH

SOURCE: PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103 <--
WO 9924460	A3	19990902		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2306313	AA	19990520	CA 1998-2306313	19981103 <--
AU 9914873	A1	19990531	AU 1999-14873	19981103 <--
AU 751669	B2	20020822		
EP 1028942	A2	20000823	EP 1998-958887	19981103 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813197	A	20000829	BR 1998-13197	19981103 <--
JP 2001522862	T2	20011120	JP 2000-520468	19981103
RU 2201420	C2	20030327	RU 2000-114821	19981103
ZA 9810073	A	19990505	ZA 1998-10073	19981104 <--
NO 2000002320	A	20000704	NO 2000-2320	20000502 <--
US 6353017	B1	20020305	US 2000-643639	20000822
PRIORITY APPLN. INFO.:			GB 1997-23407	A 19971105
			US 1997-108160P	P 19971205
			US 1997-985973	A 19971205
			WO 1998-EP6937	W 19981103
			US 1998-186223	B1 19981104

OTHER SOURCE(S): MARPAT 130:352553

AB N-terminal substituted dipeptide nitriles R(L)xx1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S; L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepd. as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-N.alpha.-(2,2-diphenylacetyl)-L-phenylalaninamide was prepd. and shown to have IC50 approx. 5 nM for inhibition of cathepsin B.

IT 215096-76-7P 215301-34-1P 225122-28-1P

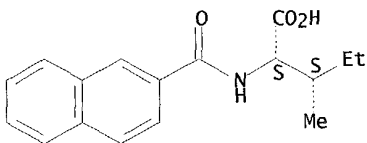
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)

RN 215096-76-7 CAPLUS

CN L-Isoleucine, N-(2-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

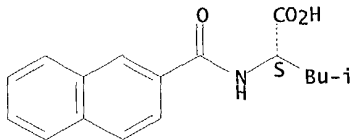


OK

RN 215301-34-1 CAPLUS

CN L-Leucine, N-(2-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

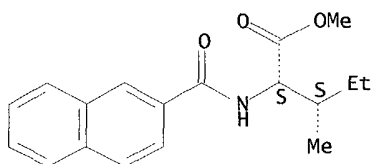
Absolute stereochemistry.



OK

RN 225122-28-1 CAPLUS
 CN L-Isoleucine, N-(2-naphthalenylcarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

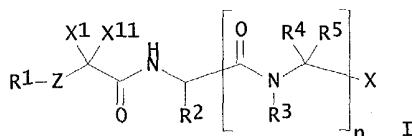
Absolute stereochemistry.



OK

L91 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1998:352863 CAPLUS
 DOCUMENT NUMBER: 129:41414
 TITLE: Preparation of N-(phenylacetyl)di- and tripeptide derivatives for inhibiting .beta.-amyloid peptide release
 INVENTOR(S): Audia, James E.; Britton, Thomas C.; Droste, James J.; Folmer, Beverly K.; Huffman, George W.; John, Varghese; Latimer, Lee H.; Mabry, Thomas E.; Nissen, Jeffrey S.; et al.
 PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; Eli Lilly & Co.; Audia, James E.; Britton, Thomas C.; Droste, James J.; Folmer, Beverly K.; Huffman, George W.; John, Varghese
 SOURCE: PCT Int. Appl., 487 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822494	A2	19980528	WO 1997-US20804	19971121 <--
WO 9822494	A3	19981126		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ZA 9710470	A	19980625	ZA 1997-10470	19971120 <--
AU 9853561	A1	19980610	AU 1998-53561	19971121 <--
EP 942924	A2	19990922	EP 1997-950601	19971121 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
CN 1238779	A	19991215	CN 1997-199803	19971121 <--
BR 9713400	A	20000125	BR 1997-13400	19971121 <--
JP 2001503782	T2	20010321	JP 1998-523756	19971121
NO 9902368	A	19990621	NO 1999-2368	19990514 <--
MX 9904744	A	20000731	MX 1999-4744	19990521 <--
PRIORITY APPLN. INFO.:			US 1996-755442	A 19961122
			US 1997-807427	A 19970228
			US 1997-807528	A 19970228
			US 1997-808528	A 19970228
			WO 1997-US20804	W 19971121
OTHER SOURCE(S):	MARPAT 129:41414			
GI				



AB Disclosed are compds. I [R1 = aryl, heteroaryl, heterocyclyl, optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, or cycloalkenyl; R2 = H, any group R1; each R3 = H, Me; R3-R4 may form optionally fused cyclic structure of 3-8 atoms; each R4 = any group R2; each R5 = H, Me; R4-R5 may form a C3-6 cycloalkyl group; X = CO-Y, CS-Y; Y = OH, aryl, heteroaryl, heterocyclyl, optionally substituted alkyl, cycloalkyl, alkoxy, thioalkoxy, amino, etc.; X1 = H, OH, F; X11 = H, OH, F; or X1X11 = O; Z = bond, O, S; n = 1, 2] and pharmaceutically acceptable salts thereof, which inhibit .beta.-amyloid peptide release and/or its synthesis, and, accordingly, have utility in treating Alzheimer's disease. Also disclosed pharmaceutical compns. comprising a compd. which inhibits .beta.-amyloid peptide release and/or its synthesis as well as methods for treating Alzheimer's disease both prophylactically and therapeutically with such pharmaceutical compns. Over 400 title compds., e.g. 3,5-F2C6H3CH2CO-L-Ala-L-Nle-OMe, were prepd. and screened for inhibition of .beta.-amyloid prodn. Formulations for pharmaceutical compns. are also given.

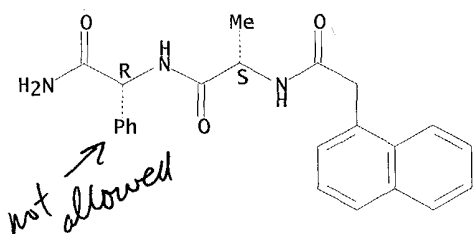
IT 208258-51-9P 208258-52-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(phenylacetyl)di- and tripeptide derivs. for inhibiting .beta.-amyloid peptide release)

RN 208258-51-9 CAPLUS

CN Glycinamide, N-(1-naphthalenylacetyl)-L-alanyl-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

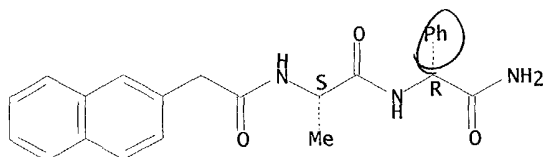
Absolute stereochemistry.



RN 208258-52-0 CAPLUS

CN Glycinamide, N-(2-naphthalenylacetyl)-L-alanyl-2-phenyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

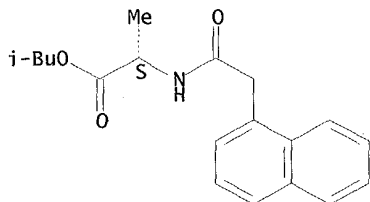


IT 208116-35-2P 208116-36-3P 208116-49-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-(phenylacetyl)di- and tripeptide derivs. for

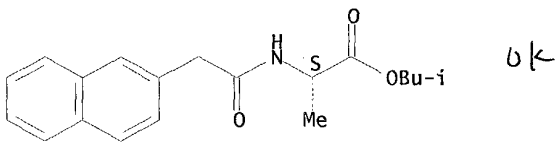
inhibiting .beta.-amyloid peptide release)
 RN 208116-35-2 CAPLUS
 CN L-Alanine, N-(1-naphthalenylacetyl)-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

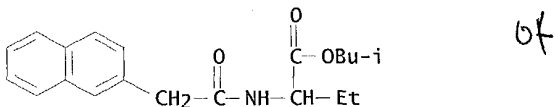


RN 208116-36-3 CAPLUS
 CN L-Alanine, N-(2-naphthalenylacetyl)-, 2-methylpropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208116-49-8 CAPLUS
 CN Butanoic acid, 2-[(2-naphthalenylacetyl)amino]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



L91 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:310423 CAPLUS

DOCUMENT NUMBER: 129:54583

TITLE: Novel HIV- protease inhibitors containing .beta.-hydroxyether and -thioether dipeptide

AUTHOR(S): isostere surrogates: modification of the P3 ligand
 Patel, Naginbhai M.; Bennett, Frank; Girijavallabhan, Viyyoor M.; Dasmahapatra, Bimalendu; Butkiewicz, Nancy; Hart, Andrea

CORPORATE SOURCE: Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(8), 931-934

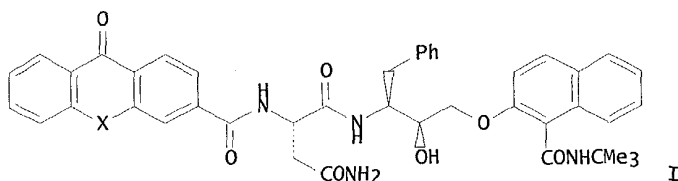
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



bod

AB Studies involving modifications to the P3 position of previously described HIV-protease inhibitors contg. .beta.-hydroxyether and thioether dipeptide isostere replacements led to the discovery of pseudopeptides I (X = CO, SO₂) with improved antiviral activities.

IT 149451-35-4P

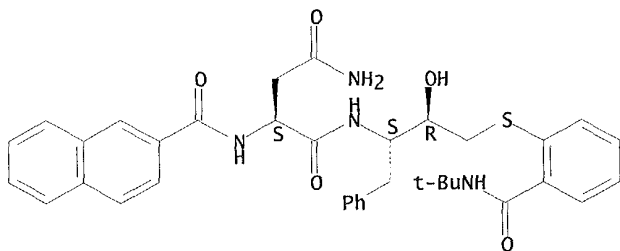
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of novel HIV protease inhibitors contg. hydroxyether and thioether dipeptide isostere surrogates)

RN 149451-35-4 CAPLUS

CN Butanediamide, N1-[(1S,2R)-3-[[2-[[[(1,1-dimethylethyl)amino]carbonyl]phenyl]thio]-2-hydroxy-1-(phenylmethyl)propyl]-2-[(2-naphthalenylcarbonyl)amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



bod

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:220603 CAPLUS

DOCUMENT NUMBER: 126:212446

TITLE: Tripeptide methyl ketone cysteine protease inhibitors for use in treatment of Ige mediated allergic diseases

INVENTOR(S): Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib, Farouk; Quibell, Martin

PATENT ASSIGNEE(S): Peptide Therapeutics Limited, UK; Johnson, Tony; Hart, Terrance; Laing, Peter; Shakib, Farouk; Quibell, Martin

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704004	A1	19970206	WO 1996-GB1707	19960717 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,				

EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR,
 LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,
 SD, SE
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM
 AU 9665242 A1 19970218 AU 1996-65242 19960717 <--
 AU 716716 B2 20000302
 EP 839155 A1 19980506 EP 1996-924976 19960717 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 JP 11509543 T2 19990824 JP 1996-506421 19960717 <--
 US 6034066 A 20000307 US 1998-45 19980226 <--
 PRIORITY APPLN. INFO.: GB 1995-14616 19950717
 GB 1995-22221 19951031
 WO 1996-GB1707 19960717

OTHER SOURCE(S): MARPAT 126:212446

AB Tripeptide compds. were prepd for use in the treatment of allergic diseases, including juvenile asthma and eczema, via inhibition of the cysteine protease activity of Dermatophagoides pteronyssinus (Der p I), a major allergen of house dust mite. Compds. claimed included R1-CONH-XR2-CONH-YR3-CONH-ZR4-W [X, Y, Z = N, CH; R1 = nitrogen blocking group; R2, R3, R4 = side-chains on X, Y, Z; W = group that reacts irreversibly with active cysteine thiol of Der p I; R1 = hydrophobic Ph, 2-naphthyl, 9-anthracyl, heteroaryl optionally connected to heteroatom to carbonyl group, etc.; XR2 = Ala, Leu, Nle, Val, etc; YR3 = Lys, Gln, Met(O), Ala; ZR4 = Ala, Leu, Nle, Val, Ile, etc.; W = E-CH2CHO, E-CH2CH:CH2, E-CH2CH:CHCHO, R-CO2NCHO, Y-CH:CH2; E = aryloxy, arylthio, heteroaryl, halo, R-SO3, R2P(O)O, RCO2; R = alkyl, aryl; Y = ester, sulfone, carboxylate, amide, etc. groups]. E64, L-trans-epoxysuccinyl-leucylamido(4-guanidino)butane, is excluded from the claimed compds. Thus, Bz-Val-Ala-Nle-OH underwent successive treatment with iso-Bu chloroformate/N-methylmorpholine, CH2N2, and HBr/HOAc to give Bz-Val-Ala-Nle-CH2Br which reacted with 2,6-Cl2C6H3CO2OH to give Bz-Val-Ala-Nle-CH2O2CC6H3Cl2-2,6 (I). In Der p I enzyme inhibiting assay, I had a Kobs/[I] of 6.8 x 107 M-1 s-1.

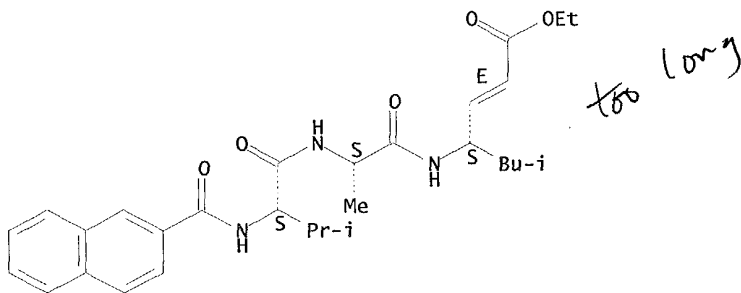
IT 187991-69-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of tripeptide Me ketones with allergen inhibiting activity)

RN 187991-69-1 CAPLUS

CN L-Alaninamide, N-(2-naphthalenylcarbonyl)-L-valyl-N-[(1S,2E)-4-ethoxy-1-(2-methylpropyl)-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L91 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:593835 CAPLUS

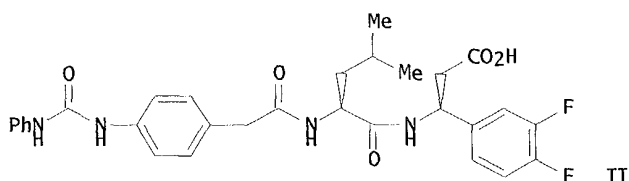
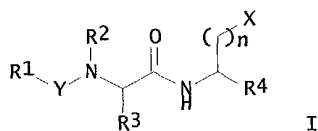
DOCUMENT NUMBER: 125:248489

TITLE: Preparation of dipeptide derivatives as cell adhesion inhibitors

INVENTOR(S): Adams, Steven P.; Lin, Ko-Chung; Lee, Wen-Cherng;

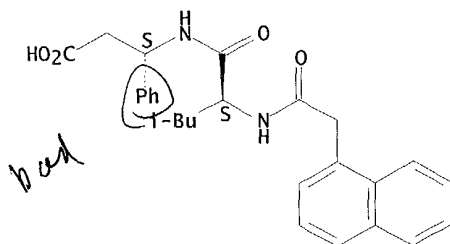
PATENT ASSIGNEE(S): Castro, Alfredo C.; Zimmerman, Craig N.; Hammond,
 SOURCE: Charles E.; Liao, Yu-Sheng; Cuervo, Julio Hernan;
 Singh, Juswinder
 Biogen, Inc., USA
 PCT Int. Appl., 169 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622966	A1	19960801	WO 1996-US1349	19960118 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
US 6306840	B1	20011023	US 1995-376372	19950123
CA 2211181	AA	19960801	CA 1996-2211181	19960118 <--
AU 9649115	A1	19960814	AU 1996-49115	19960118 <--
AU 718926	B2	20000504		
EP 805796	A1	19971112	EP 1996-905316	19960118 <--
EP 805796	B1	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
BR 9606778	A	19980106	BR 1996-6778	19960118 <--
CN 1177343	A	19980325	CN 1996-192270	19960118 <--
JP 10513160	T2	19981215	JP 1996-523071	19960118 <--
EP 1142867	A2	20011010	EP 2001-107877	19960118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
AT 229498	E	20021215	AT 1996-905316	19960118
ES 2183937	T3	20030401	ES 1996-905316	19960118
CZ 291556	B6	20030416	CZ 1997-2340	19960118
TW 500714	B	20020901	TW 1996-85100690	19960122
NO 9703384	A	19970919	NO 1997-3384	19970722 <--
FI 9703087	A	19970922	FI 1997-3087	19970722 <--
BG 63383	B1	20011231	BG 1997-101841	19970821
US 6376538	B1	20020423	US 1997-875321	19970919
US 2003083267	A1	20030501	US 2001-935461	20010822
US 2003018016	A1	20030123	US 2001-2341	20011023
PRIORITY APPLN. INFO.:				
US 1995-376372 A2 19950123				
EP 1996-905316 A3 19960118				
WO 1996-US1349 W 19960118				
US 1997-875321 A3 19970919				
OTHER SOURCE(S): MARPAT 125:248489				
GI				



- AB Novel dipeptide analogs I [X = CO₂H, PO₃H⁻, SO₂R⁵, SO₃H, OPO₃H⁻, CO₂R⁴, CONR⁴; Y = CO, SO₂, PO₂; n = 0-2; R¹ = optionally substituted alkyl, alkenyl, alkynyl, aryl-fused cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl, alkoxy, alkenyloxy, aralkoxy, alkylamino, alkenylamino, alkynylamino, aryloxy, arylamino, N-alkylurea-substituted alkyl, heterocyclyl; R² = H, aryl, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl-substituted alkyl; R²NCR³ = heterocyclic ring; R³ = natural, unnatural, modified, or substituted amino acid side chain; R⁴ = optionally substituted aryl, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl-substituted alkyl, H, heterocyclyl, heterocyclylcarbonyl, aminocarbonyl, amido, alkylaminocarbonyl, arylaminocarbonyl, acylaminocarbonyl, acyl; R⁵ = alkyl, alkenyl, cycloalkyl, cycloalkenyl, aryl, aralkyl, aralkenyl, aralkynyl] are prepd. as compds. useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical compns. of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, .beta.-amino acid-contg. dipeptide II, prepd. by std. methods, displayed an IC₅₀ of <50 nM in a cell adhesion inhibition assay.
- IT 181520-01-4P 181520-03-6P 181520-87-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. of .beta.-amino acid dipeptide derivs. as cell adhesion inhibitors)
- RN 181520-01-4 CAPLUS
- CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(1-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

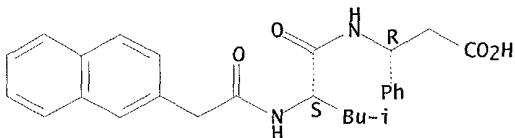
Absolute stereochemistry.



RN 181520-03-6 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

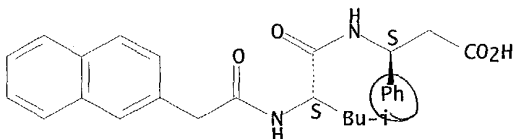
Absolute stereochemistry.



RN 181520-87-6 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



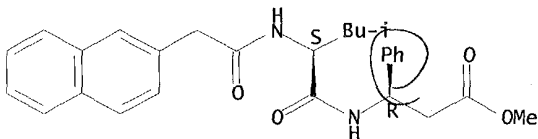
IT 181518-17-2P 181518-19-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of .beta.-amino acid dipeptide derivs. as cell adhesion inhibitors)

RN 181518-17-2 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

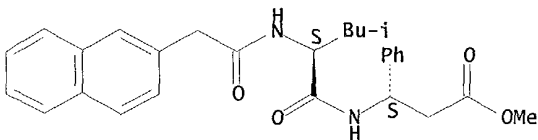
Absolute stereochemistry.



RN 181518-19-4 CAPLUS

CN Benzenepropanoic acid, .beta.-[[[(2S)-4-methyl-2-[(2-naphthalenylacetyl)amino]-1-oxopentyl]amino]-, methyl ester, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib abs hitstr 11-25

L91 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:544115 CAPLUS

DOCUMENT NUMBER: 125:237576

TITLE: Novel Peptidyl .alpha.-Keto Amide Inhibitors of Calpains and Other Cysteine Proteases

AUTHOR(S): Li, Zhaozhao; Ortega-Vilain, Anne-Cecile; Patil, Girish S.; Chu, Der-Lun; Foreman, J. E.; Eveleth, David D.; Powers, James C.

CORPORATE SOURCE: School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA

SOURCE: Journal of Medicinal Chemistry (1996), 39(20), 4089-4098

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of new dipeptidyl .alpha.-keto amides of the general structure R1-L-Leu-D,L-AA-CONH-R2 were synthesized and evaluated as inhibitors for the cysteine proteases calpain I, calpain II, and cathepsin B. They combine 10 different N-protecting groups (R1), 3 amino acids residues in P1 (AA), and 44 distinct substituents on the .alpha.-keto amide nitrogen (R2). In general, calpain II was more sensitive to these inhibitors than calpain I, with a large no. of inhibitors displaying disso. consts. (K_i) in the 10-100 nM range. Calpain I was also effectively inhibited, but very low K_i values were obsd. with a smaller no. of inhibitors than with calpain II. Cathepsin B was weakly inhibited by most compds. in this study. The best inhibitors for calpain II were Z-Leu-Abu-CONH-CH₂-CHOH-C₆H₅ (K_i = 15 nM), Z-Leu-Abu-CONH-CH₂-2-pyridyl (K_i = 17 nM), and Z-Leu-Abu-CONH-CH₂-C₆H₃(3,5(OMe)₂) (K_i = 22 nM). The best calpain I inhibitor in this study was Z-Leu-Nva-CONH-CH₂-2-pyridyl (K_i = 19 nM). The peptide .alpha.-keto amide Z-Leu-Abu-CONH-(CH₂)₂-3-indolyl was the best inhibitor for cathepsin B (K_i = 31 nM). Some compds. acted as specific calpain inhibitors, with comparable activity on both calpains I and II and a lack of activity on cathepsin B. Others were specific inhibitors for calpain I (e.g., 73) or calpain II. Such inhibitors may be useful in elucidating the physiol. and pathol. events involving these proteases and may become possible therapeutic agents.

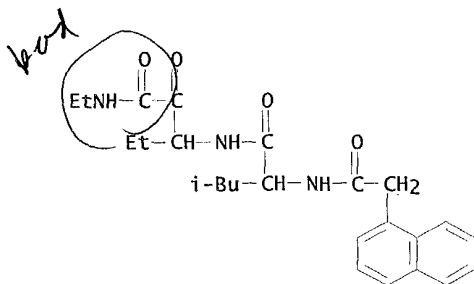
IT 178675-63-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of novel peptidyl .alpha.-keto amide inhibitors of calpains and other cysteine proteases)

RN 178675-63-3 CAPLUS

CN 1-Naphthaleneacetamide, N-[1-[[[1-ethyl-3-(ethylamino)-2,3-dioxopropyl]amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)



L91 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:887871 CAPLUS

DOCUMENT NUMBER: 123:340965

TITLE: Preparation of dipeptide analogs as endothelin receptor antagonists.

Searched by Susan Hanley 305-4053

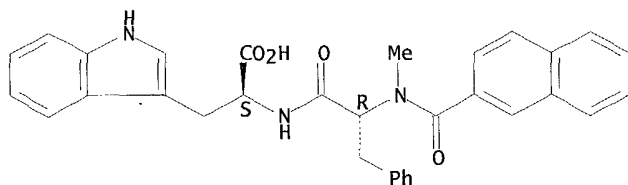
KAM 09/926,391

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dipeptide analogs as endothelin receptor
antagonists)

RN 169544-93-8 CAPLUS

CN L-Tryptophan, N-[N-methyl-N-(2-naphthalenylcarbonyl)-D-phenylalanyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



good

Exp 21

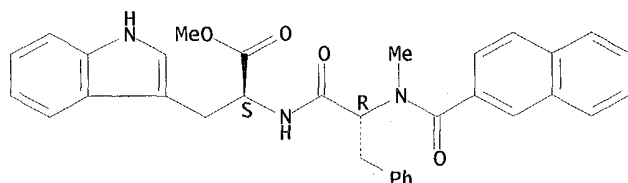
IT 169546-10-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of dipeptide analogs as endothelin receptor
antagonists)

RN 169546-10-5 CAPLUS

CN L-Tryptophan, N-[N-methyl-N-(2-naphthalenylcarbonyl)-D-phenylalanyl]-,
methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



good

L91 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:758608 CAPLUS

DOCUMENT NUMBER: 123:170184

TITLE: New pseudo-dipeptide derivatives, their
preparation, and their use as gastrin antagonists.

INVENTOR(S): Martinez, Jean; Riquet, William; Bigg, Dennis; Halazy,
Serge

PATENT ASSIGNEE(S): Fabre Pierre Medicament, Fr.

SOURCE: Fr. Demande, 36 pp.

CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2697843	A1	19940513	FR 1992-13542	19921110 <--
WO 9411390	A1	19940526	WO 1993-FR1099	19931109 <--

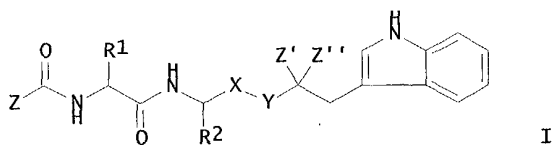
W: CA, JP, US

Rw: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

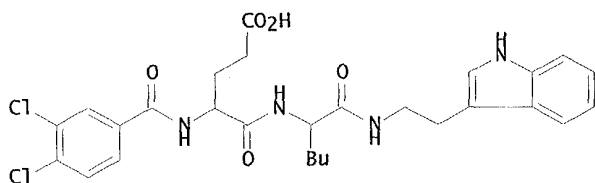
PRIORITY APPLN. INFO.: FR 1992-13542 19921110

OTHER SOURCE(S): MARPAT 123:170184

GI



I



II

AB Title compds. I [Z = (un)substituted Ph, PhCH₂, indanyl, (poly)cycloalkyl, indolylalkyl, naphthyl, naphthylmethyl, PhOCH₂, naphthoxymethyl; R₁ = (CH₂)_nCO₂H; n = 1-5; R₂ = alkyl; X = NH or CO; Y = CO or NH; X .noteq. Y; Z' = H, Me; Z'' = H, CO₂R₃, NHCOR₃; if Y = NH, Z'' .noteq. NHCOR₃; if Y = CO, Z'' .noteq. COR₃; R₃ = (un)substituted alkyl, (poly)cycloalkyl, Ph] and salts are claimed and prepd. (14 examples). I are gastrin and CCK receptor antagonists, and are claimed useful for treating ulcers, Zollinger-Ellison syndrome, and reflux-induced esophagitis. For example, amidation of tryptamine with Boc-D-Nle-OSu [Boc = tert-BuOCO, Su = N-succinimidyl] in DMF gave 79% Boc-D-Nle-NHCH₂CH₂R [R = 3-indolyl]. This was deprotected with CF₃CO₂H and coupled with Z-D-Glu(OCH₂Ph)-ONp [Z = PhCH₂OCO, Np = C₆H₄NO₂-p] in DMF in the presence of HOBT and DIEA to give 94% Z-D-Glu(OCH₂Ph)-D-Nle-NHCH₂CH₂R. Hydrogenolysis of the latter compd. and coupling with 3,4-Cl₂C₆H₃CO₂Su in DMF in the presence of DIEA gave title compd. D,D-II. In the EtOH-induced ulcer test in mice, this compd. gave 80% inhibition at 25 mg/kg p.o.

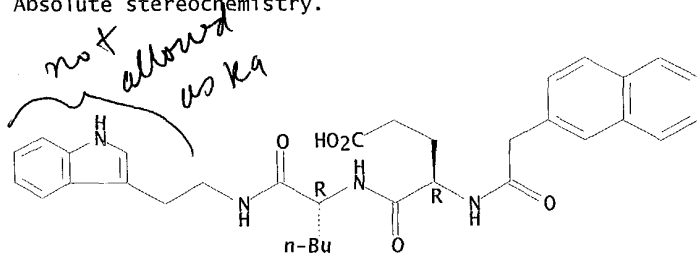
IT 166945-25-1P 166945-26-2P 166945-27-3P
166945-28-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pseudo-dipeptides as gastrin and CCK antagonists)

RN 166945-25-1 CAPLUS

CN D-Norleucinamide, N-(2-naphthalenylacetyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

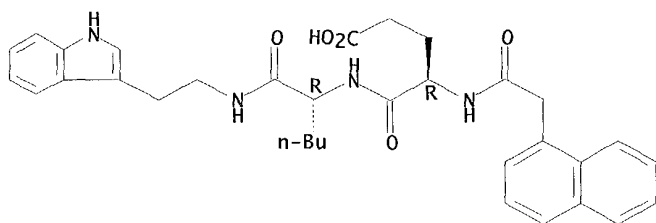
Absolute stereochemistry.



RN 166945-26-2 CAPLUS

CN D-Norleucinamide, N-(1-naphthalenylacetyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

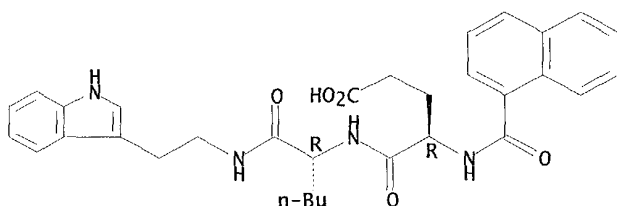
Absolute stereochemistry.



RN 166945-27-3 CAPLUS

CN D-Norleucinamide, N-(1-naphthalenylcarbonyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

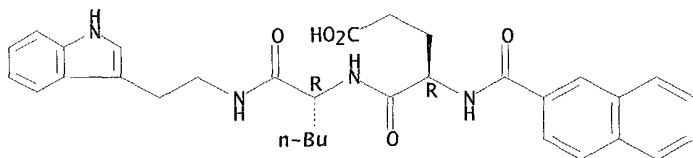
Absolute stereochemistry.



RN 166945-28-4 CAPLUS

CN D-Norleucinamide, N-(2-naphthalenylcarbonyl)-D-.alpha.-glutamyl-N-[2-(1H-indol-3-yl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:245758 CAPLUS

DOCUMENT NUMBER: 120:245758

TITLE: 2-NAP: a selective, hydrophilic, non-peptide CCKA - receptor antagonist derived from the cholecystokinin C-terminal dipeptide

AUTHOR(S): McDonald, Iain M.; Bodkin, Michael J.; Broughton, Howard B.; Dunstone, David J.; Kalindjian, S. Barret; Low, Caroline M. R.

CORPORATE SOURCE: Sch. Med. Dent., King's Coll., London, SE24 9JE, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1993), 3(8), 1511-16

CODEN: BMCLE8; ISSN: 0960-894X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Analogs of the cholecystokinin (CCK) C-terminal dipeptide(32-33) (H-Asp-Phe-NH₂) have been prepd. and the structure-activity relationships of this series are described. The sodium salt of 2-naphthalenesulfonyl-L-aspartyl (2-phenethyl)amide, (2-NAP), displayed high affinity for CCKA receptors by its antagonism of CCK8-stimulated guinea-pig gallbladder contraction. In addn., 2-NAP exhibits selectivity with respect to

gastrin/CCKB receptors (>300-fold) and has a low log P (-0.91, chloroform/buffer).

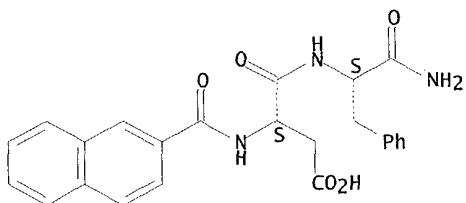
IT 154510-45-9 154510-51-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(cholecystokinin A receptor antagonist activity of)

RN 154510-45-9 CAPLUS

CN L-Phenylalaninamide, N-(2-naphthalenylcarbonyl)-L-.alpha.-aspartyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

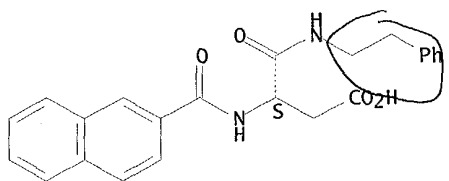


good

RN 154510-51-7 CAPLUS

CN Butanoic acid, 3-[(2-naphthalenylcarbonyl)amino]-4-oxo-4-[(2-phenylethyl)amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



bad

L91 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1993:496186 CAPLUS

DOCUMENT NUMBER: 119:96186

TITLE: Preparation of pseudopeptides and **dipeptides** characterized by a substituted methyl ketone moiety at the C-terminus as thiol protease inhibitors

INVENTOR(S): Ando, Ryoichi; Ando, Naoko; Masuda, Hirokazu; Morinaka, Yasuhiro; Takahashi, Chizuko; Tamao, Yoshikuni; Tobe, Akihiro

PATENT ASSIGNEE(S): Mitsubishi Kasei Corp., Japan

SOURCE: Eur. Pat. Appl., 218 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

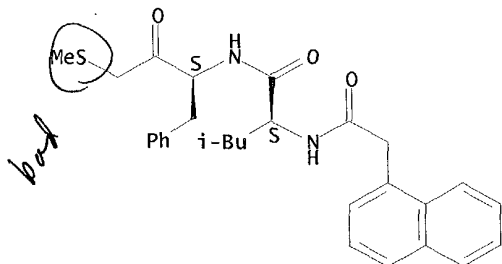
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

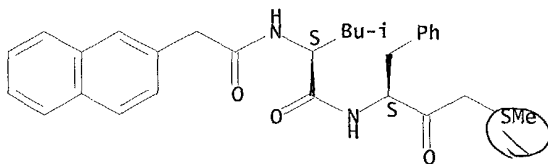
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 525420	A1	19930203	EP 1992-111129	19920701 <--
EP 525420	B1	19990512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
JP 05246968	A2	19930924	JP 1992-165094	19920623 <--
JP 3190431	B2	20010723		
CA 2072834	AA	19930102	CA 1992-2072834	19920630 <--
AT 179974	E	19990515	AT 1992-111129	19920701 <--
ES 2132096	T3	19990816	ES 1992-111129	19920701 <--
US 5639783	A	19970617	US 1995-451720	19950526 <--

Absolute stereochemistry.



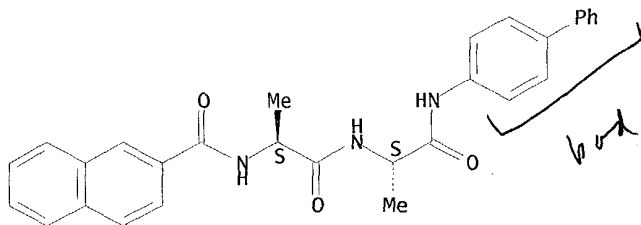
Absolute stereochemistry.



Page 32

field
 AUTHOR(S): Wall, Craig G.; Healy, Eamonn F.; Fox, Marye Anne
 CORPORATE SOURCE: Dep. Chem., Univ. Texas, Austin, TX, 78712, USA
 SOURCE: International Journal of Quantum Chemistry (1992), 44(4), 543-8
 CODEN: IJQCB2; ISSN: 0020-7608
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A conformational anal. of the dipeptide 2-C₁₀H₇CO-Ala-Ala-NHC₆H₄Ph-4 (I) was performed using a std. mol. mechanics force field. to explain obsd. electron transfer rates between the terminal arom. moieties. The resulting low-energy conformers could conveniently be grouped into two families with an av. energy difference of ca. 2 kcal mol⁻¹ and populations of 64% and 30%, resp. These results correlate well with the 78:22 ratio of the two exptl. distinguishable decay processes for the radical anion of I.
 IT 135311-05-6
 RL: PROC (Process)
 (conformational anal. of, by mol. mechanics)
 RN 135311-05-6 CAPLUS
 CN L-Alaninamide, N-(2-naphthalenylcarbonyl)-L-alanyl-N-[1,1'-biphenyl]-4-yl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1993:806 CAPLUS
 DOCUMENT NUMBER: 118:806
 TITLE: Method of treating benign and malignant proliferative skin disease by topical administration of a somatostatin analog
 INVENTOR(S): Bogden, Arthur E.; Moreau, Jacques Pierre
 PATENT ASSIGNEE(S): Biomeasure, Inc., USA
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9213554	A1	19920820	WO 1992-US1027	19920207 <--
W: CA, CS, FI, HU, JP, NO, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 542934	A1	19930526	EP 1992-906420	19920207 <--
EP 542934	B1	19990616		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 05506254	T2	19930916	JP 1992-505872	19920207 <--
AT 181240	E	19990715	AT 1992-906420	19920207 <--
ES 2134798	T3	19991016	ES 1992-906420	19920207 <--
US 6087337	A	20000711	US 1993-89410	19930709 <--
PRIORITY APPLN. INFO.:				
			US 1991-652863	A 19910208
			WO 1992-US1027	W 19920207

OTHER SOURCE(S): MARPAT 118:806

AB A compn. for treating a mammal suffering from benign or malignant proliferative skin disease comprises an effective amt. of a somatostatin analog contg. 6 amino acids, formulated with an excipient suitable for topical administration to the mammal. D-beta-Naphthyl-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂ was synthesized on benzhydrylamine-polystyrene resin. B16-F10 melanoma xenografts in mice were treated with topical somatuline.

IT 113294-82-9P

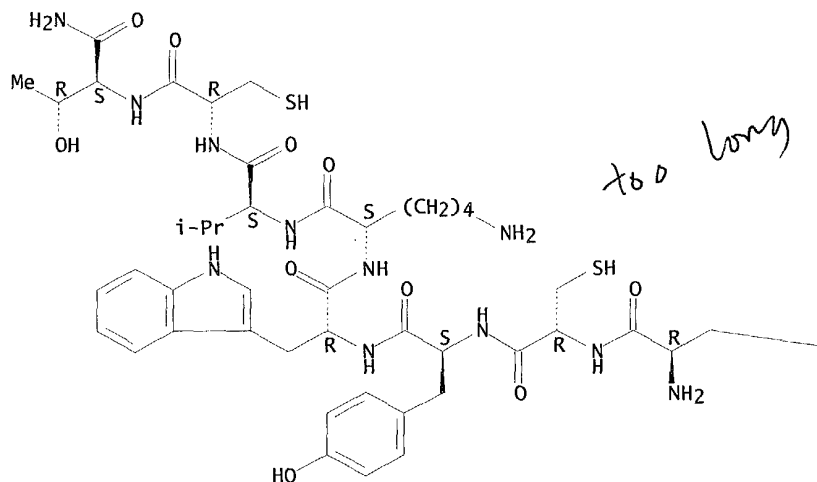
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for treatment of benign or malignant proliferative skin disease)

RN 113294-82-9 CAPLUS

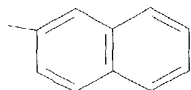
CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

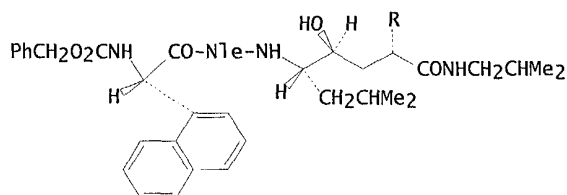
PAGE 1-A



PAGE 1-B



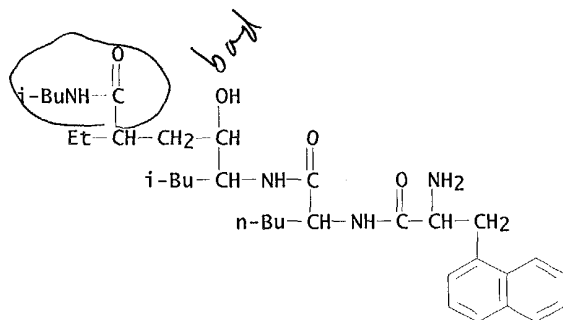
L91 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1992:470294 CAPLUS
 DOCUMENT NUMBER: 117:70294
 TITLE: Renin inhibitors. I. Synthesis and structure-activity relationships of transition-state inhibitors containing homostatine analogs at the scissile bond
 AUTHOR(S): Atsumi, Shugo; Nakano, Masato; Koike, Yutaka; Tanaka, Seichi; Matsuyama, Kenji; Nakano, Makiko; Morishima, Hajime
 CORPORATE SOURCE: Explor. Res. Lab., Banyu Pharm. Co., Ltd., Tokyo, 153, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (1992), 40(2), 364-70
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB The synthesis and structure-activity relationships of transition-state renin inhibitors, e.g. I [R = H, Me, Et, Pr, CHMe2, CH2CHMe2, Me3CO2CNHCH2, HOCH2CH2, HOCH2CH2CH2, H2NCH2CH2CH2 HOCHMeCH2, HOCH2CH(OH)CH2], contg. the homostatine analogs at the scissile bond are described. These inhibitors incorporate the amino acid side chains corresponding to positions 7-12 (P4-P2') of angiotensinogen. Et, 2-hydroxyethyl, and 3-hydroxypropyl groups at position 2 of the homostatine analogs (P1') are more effective for increasing potency than the iso-Pr group. A combination of residues at P1, P3, and P4 is important for potency and this result suggests that S1, S3, and S4 form a huge hydrophobic core together in renin.

IT 141713-99-7 141714-04-7 141782-86-7
 141783-51-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (renin inhibitory activity of)

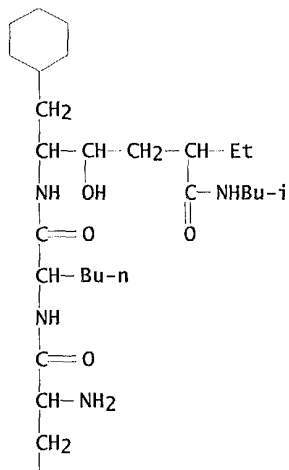
RN 141713-99-7 CAPLUS
 CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4S*)]- (9CI) (CA INDEX NAME)



RN 141714-04-7 CAPLUS

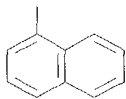
CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-4-[[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]-(9CI) (CA INDEX NAME)

PAGE 1-A



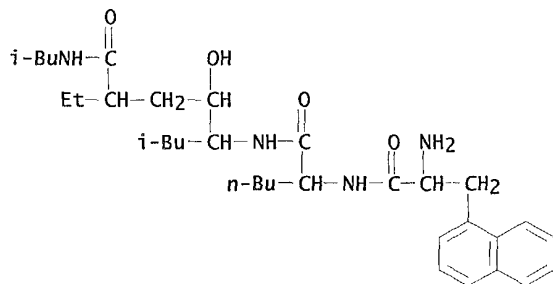
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PAGE 2-A



RN 141782-86-7 CAPLUS

CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[2-hydroxy-1-(2-methylpropyl)-4-[[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4R*)]-(9CI) (CA INDEX NAME)

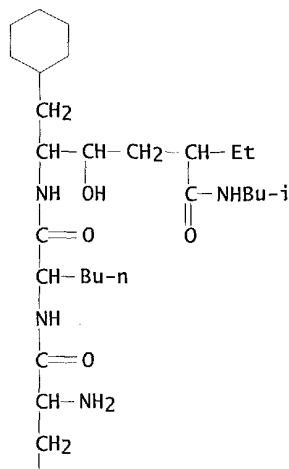


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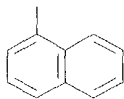
RN 141783-51-9 CAPLUS

CN L-Norleucinamide, 3-(1-naphthalenyl)-L-alanyl-N-[1-(cyclohexylmethyl)-2-hydroxy-4-[[[(2-methylpropyl)amino]carbonyl]hexyl]-, [1S-(1R*,2R*,4S*)]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L91 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:256009 CAPLUS

DOCUMENT NUMBER: 116:256009

TITLE: Development of potent and selective CCK-A receptor agonists from Boc-CCK-4: tetrapeptides containing Lys(N.epsilon.)-amide residues

AUTHOR(S): Shiosaki, Kazumi; Lin, Chun Wei; Kopecka, Hana; Craig, Richard A.; Bianchi, Bruce R.; Miller, Thomas R.; Witte, David G.; Stashko, Michael; Nadzan, Alex M.

CORPORATE SOURCE: Neurosci. Res. Div., Abbott Lab., Abbott Park, IL, 60064, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(11), 2007-14

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of Boc-CCK-4 (Boc = CO₂Me₃) derivs. represented by the general structure Boc-Trp-Lys(COR)Asp-Phe-NH₂, where R is an arom., heterocyclic, or aliph. group, are potent and selective CCK-A receptor agonists. These amide-bearing compds. complement the previously described urea-based tetrapeptides (Shiosaki et al. 1991); structure activity studies revealed parallel as well as divergent trends between these two series. A significant correlation was obsd. between pancreatic binding affinity and the resonance const. ρ of the Ph substituent in one particular series of derivs. Sulfation of phenolic amides appended onto the ϵ -amino group of the lysine did not affect affinity for the CCK-A receptor in contrast to the 500-fold increase in binding potency obsd. upon sulfation of CCK-8, suggesting that the lysine appendage and the sulfated tyrosine in CCK-8, both key structural elements that impart high affinity for the CCK-A receptor, are interacting differently with the receptor. The amide-bearing tetrapeptides are full agonists relative to

CCK-8 in stimulating pancreatic amylase release while being partial agonists in eliciting phosphoinositide (PI) hydrolysis. Both effects were blocked by selective CCK-A receptor antagonists.

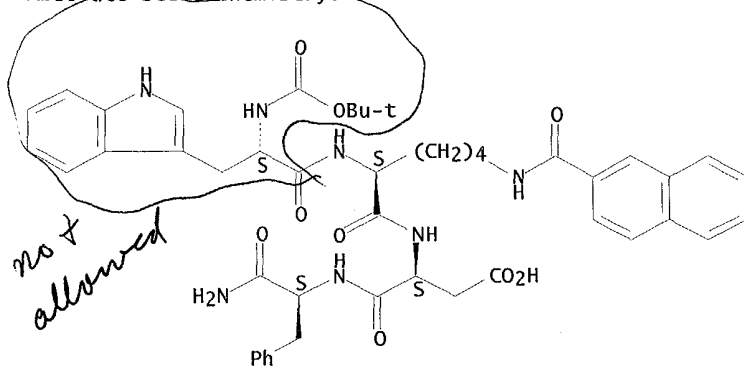
IT 131449-07-5P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as selective CCK-A receptor agonist)

RN 131449-07-5 CAPLUS

CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-N6-(2-naphthalenylcarbonyl)-L-lysyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:152363 CAPLUS

DOCUMENT NUMBER: 116:152363

TITLE: Conformational preferences of oligopeptides rich in .alpha.-aminoisobutyric acid. I. Observation of a 310/.alpha.-helical transition upon sequence permutation

AUTHOR(S): Basu, Gautam; Bagchi, Ken; Kuki, Atsuo
CORPORATE SOURCE: Dep. Chem., Cornell Univ., Ithaca, NY, 14853, USA

SOURCE: Biopolymers (1991), 31(14), 1763-74

CODEN: BIPMAA; ISSN: 0006-3525

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The soln. conformation of peptides rich in .alpha.-aminoisobutyric acid (Aib) is a subtle problem, not because of helix/coil transitions, but rather because of .alpha.-helical/310-helical competition. A series of peptides contg. 75% Aib has been synthesized that feature identical amino acid compn. but differing sequences; they are sequence permutation isomers. NMR hydrogen-bonding studies reveal that there is a sequence permutation-induced transition between the 2 alternative helical forms within this set. The implications for the design and conformational prediction of helical Aib-rich peptides are discussed.

IT 139881-89-3

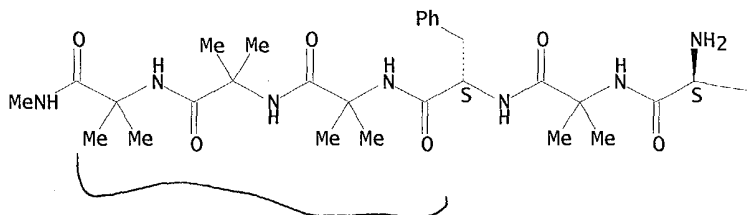
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with aminoisobutyric acid dipeptide oxazolone)

RN 139881-89-3 CAPLUS

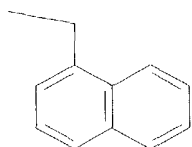
CN Alaninamide, 3-(1-naphthalenyl)-L-alanyl-2-methylalanyl-L-phenylalanyl-2-methylalanyl-2-methylalanyl-N,2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

W^b

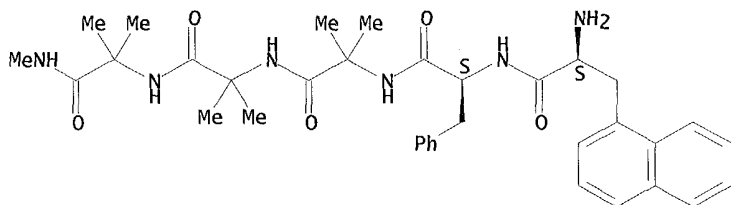
IT 139881-88-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of, with aminoisobutyric acid tripeptide)

RN 139881-88-2 CAPLUS

CN Alaninamide, 3-(1-naphthalenyl)-L-alanyl-L-phenylalanyl-2-methylalanyl-2-methylalanyl-N,2-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:498001 CAPLUS

DOCUMENT NUMBER: 113:98001

TITLE: Novel inhibitors of human renin unrelated to the
angiotensinogen sequence. Analogs of a tetrapeptide,
Boc-D-Phe-Cys(Acm)-D-Trp-Leu-OMeAUTHOR(S): Dutta, Anand S.; Gormley, James J.; McLachlan, Peter
F.; Major, John S.CORPORATE SOURCE: Chem. Dep., ICI Pharm., Macclesfield/Cheshire, SK10
4TG, UKSOURCE: Journal of Chemical Research, Synopses (1990
, (1), 2-3

CODEN: JRPSDC; ISSN: 0308-2342

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Eighty-three title peptides analogs were prepd. by conventional soln.
methods. Renin-inhibiting activation were detd. and structure-activity
relationships were discussed.

IT 128730-83-6P

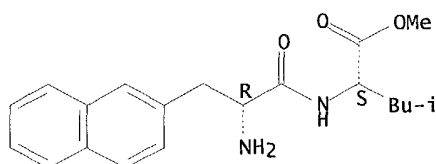
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(prepn. and peptide coupling of, with cysteine deriv.)

RN 128730-83-6 CAPLUS

CN L-Leucine, N-[3-(2-naphthalenyl)-D-alanyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:478951 CAPLUS

DOCUMENT NUMBER: 113:78951

TITLE: Angiotensin-converting enzyme inhibitors: synthesis and biological activity of N-substituted tripeptide inhibitors

AUTHOR(S): Sawayama, Tadahiro; Tsukamoto, Masatoshi; Sasagawa, Takashi; Nishimura, Kazuya; Deguchi, Takashi; Takeyama, Kunihiko; Hosoki, Kanoo

CORPORATE SOURCE: Res. Lab., Dainippon Pharm. Co., Ltd., Suita, 564, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1990), 38(1), 110-15

CODEN: CPBTAL; ISSN: 0009-2363

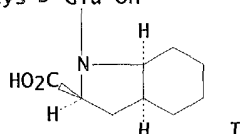
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 113:78951

GI

RCO-Lys-D-Glu-OH



AB A new series of highly potent angiotensin-converting enzyme inhibitors, 1-(N2-substituted L-lysyl-.gamma.-D-glutamyl)octahydro-1H-indole-2-carboxylic acids I (R = aryl, aralkyloxy, cycloalkyloxy, amino) was prepd.; various acyl groups were introduced at the .alpha.-amino group of the N-terminal lysine. The effect of the N2-acyl groups on in vitro inhibitory activity and oral antihypertensive effect was examd. All of the synthesized N-acyl tripeptides have in vitro inhibitory activity at an approx. nanomolar level, and showed antihypertensive potency in renal hypertensive rats at a dose of 10 mg/kg, when administered orally. Among them, compds. I (R = 2-ClC6H4CH2O, 2-FC6H4CH2O, 4-FC6H4, 4-HOC6H4, 3-pyridyl) showed potent and long-lasting antihypertensive effects compared with enalapril. Their structure-activity relationships are also discussed.

IT 128595-16-4P 128595-17-5P

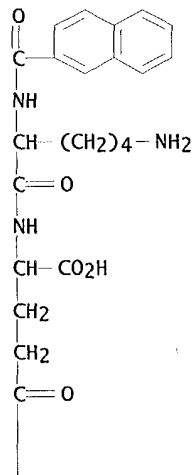
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and inhibition by, of angiotensin-converting enzyme)

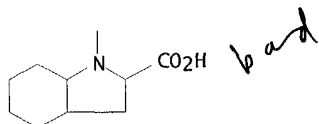
RN 128595-16-4 CAPLUS

CN D-Norvaline, 5-(2-carboxyoctahydro-1H-indol-1-yl)-N-[N2-(2-naphthalenylcarbonyl)-L-lysyl]-5-oxo-, [2S-(2.alpha.,3a.beta.,7a.beta.)]-(9CI) (CA INDEX NAME)

PAGE 1-A

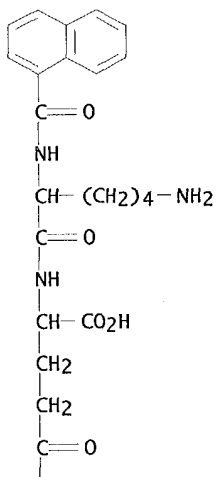


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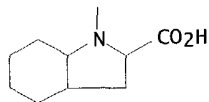


RN 128595-17-5 CAPLUS
 CN D-Norvaline, 5-(2-carboxyoctahydro-1H-indol-1-yl)-N-[N2-(1-naphthalenylcarbonyl)-L-lysyl]-5-oxo-, [2S-(2.alpha.,3a.beta.,7a.beta.)]-(9CI) (CA INDEX NAME)

PAGE 1-A

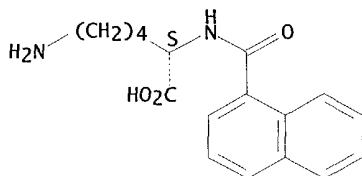


PAGE 2-A



L91 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1990:406799 CAPLUS
 DOCUMENT NUMBER: 113:6799
 TITLE: Molecular design of inverted-aspartame-type sweeteners
 AUTHOR(S): Noshio, Yasuharu; Seki, Takashi; Kondo, Miyuki; Ohfuji, Takehiko; Tamura, Masahiro; Okai, Hideo
 CORPORATE SOURCE: Fac. Eng., Hiroshima Univ., Higashi-Hiroshima, 724, Japan
 SOURCE: Journal of Agricultural and Food Chemistry (1990), 38(6), 1368-73
 CODEN: JAFCAU; ISSN: 0021-8561
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of inverted aspartame-type sweeteners, e.g. $\text{PhCO}(\text{CH}_2)_n\text{-X-Lys-OH}$ (I; $n = 0-2$; X = bond, Gly, β -Ala, Ala, $\text{NHCH}_2\text{CH}_2\text{CO}$, NHCH_2CO) were prepd. and tested for sweetness potency. I ($n = 1$, X = Gly) was 50 times as sweet as sucrose. These sweeteners are useful because the lack of ester functions increases stability in soln. and lowers toxicity.
 IT 126327-80-8P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and sweetness of)
 RN 126327-80-8 CAPLUS
 CN L-Lysine, N2-(1-naphthalenylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1988:94921 CAPLUS
 DOCUMENT NUMBER: 108:94921
 TITLE: Amino acids and peptides. XVII. Synthesis of a tridecapeptide corresponding to the sequence 165-177 of T-kininogen (tryptic peptide) containing Gln-Val-Val-Ala-Gly sequence and the relationship between structure and effect on thiol proteinase
 AUTHOR(S): Teno, Naoki; Tsuboi, Satoshi; Okada, Yoshio; Itoh, Norio; Okamoto, Hiroshi
 CORPORATE SOURCE: Fac. Pharm. Sci., Kobe-Gakuin Univ., Kobe, 673, Japan
 SOURCE: Chemical & Pharmaceutical Bulletin (1987), 35(9), 3853-8
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 108:94921
 GI

H-Ser-Ala-His-Ser-Gln-Val-Val-

Ala-Gly-Met-Asn-Tyr-Lys-OH

I

AB The title tridecapeptide I was prepd. by conventional soln. methods. Although Z-Gln-Val-Val-Ala-Gly-OMe showed inhibitory activity towards papain and protective activity against T-kininogen-induced inhibition of papain, the tryptic peptide obtained did not exhibit any effect on thiol proteinase. In order to study the relationship between structure and effect on thiol proteinase, R-Gln-Val-Val-Ala-Gly-OMe (II; R = Me₃CO₂C, H, Ac, Bz, .beta.-naphthoyl) were prepd. II (R = Bz, .beta.-naphthoyl) exhibited weak inhibitory and significant protective activities. A small peptide such as Gln-Val-Val-Ala-Gly might be better able to approach papain than I and the arom. ring assocd. with Gln-Val-Val-Ala-Gly at the N-terminus apparently strengthened the binding ability of the peptide to papain.

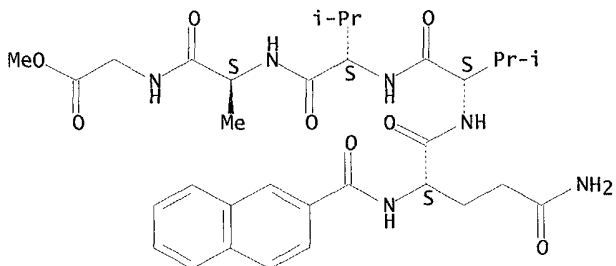
IT 112953-00-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and effect of, on papain)

RN 112953-00-1 CAPLUS

CN Glycine, N-[N-[N-[N-(2-naphthalenylcarbonyl)-L-glutaminy]-L-valyl]-L-valyl]-L-alanyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



too long

L91 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1986:479373 CAPLUS

DOCUMENT NUMBER: 105:79373

TITLE: Histidine derivatives as renin inhibitors

INVENTOR(S): Iizuka, Kinji; Kamijo, Tetsuhide; Kubota, Tetsuhiro;

Akahane, Kenji; Umeyama, Hideaki; Kiso, Yoshiaki

PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 108 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 181110	A2	19860514	EP 1985-307555	19851018 <---
EP 181110	A3	19880511		
R: BE, DE, FR, GB, IT, LU, NL, SE				
JP 61100595	A2	19860519	JP 1984-221853	19841022 <---
JP 05037422	B4	19930603		
JP 61137896	A2	19860625	JP 1984-260453	19841210 <---
JP 05037423	B4	19930603		
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US 4863904	A	19890905	US 1985-789597	19851021 <---

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US 4656269	B1	19890829	US 1988-90001688	19880110	<--
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			JP 1984-260453	19841210	
			JP 1984-271303	19841222	
			JP 1986-79726	19850415	
			US 1986-852260	19860415	

OTHER SOURCE(S): CASREACT 105:79373

AB Histidine-contg. dipeptide derivs. are prepd. as proteinase-resistant renin inhibitors useful for oral treatment of renin-assocd. hypertension. For example, N-[2-(1-naphthylmethyl)-3-(phenethylcarbamoyl)propionyl]-L-histidyl-L-leucinal (I) (100 mg/kg orally) produced a 12-16% decrease in blood pressure within 2-3 h in high-renin (furosemide-treated) marmosets. To prep. I, 1-naphthaldehyde and Et succinate were condensed and converted in 2 steps to 2-(1-naphthylmethylene)succinic anhydride, condensed with phenethylamine to 2-(1-naphthylmethylene)-3-(phenethylcarbamoyl)propionic acid, hydrogenated over Pd/C, and the product was condensed with a L-histidyl-L-leucinal semicarbazone in the presence of diphenylphosphoryl azide.

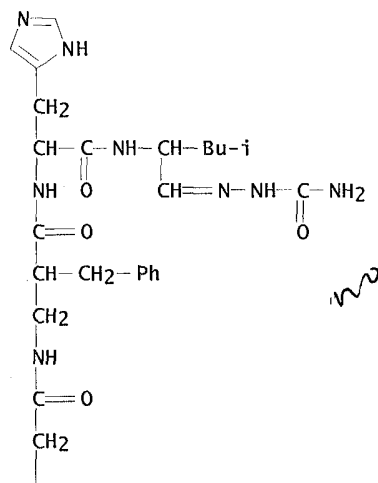
IT 103633-13-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)

RN 103633-13-2 CAPLUS

CN L-Histidinamide, N-(1-naphthalenylacetyl)-2-(phenylmethyl)-.beta.-alanyl-N-[1-[[[aminocarbonyl]hydrazono]methyl]-3-methylbutyl]-, (S)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

